

WHAT IS CLAIMED IS:

1. A method of inhibiting or neutralizing TALL-1 polypeptide biological activity in mammalian cells, comprising exposing said mammalian cells to an effective amount of TALL-1 polypeptide  
5 antagonist.

2. The method of claim 1 wherein said TALL-1 polypeptide comprises a native sequence TALL-1 polypeptide having the amino acid sequence of Figure 3 (SEQ ID NO:6) or a fragment thereof which  
10 exhibits a biological activity of the native sequence TALL-1 polypeptide shown in Figure 3 (SEQ ID NO:6).

3. The method of claim 1 wherein said TALL-1 polypeptide antagonist comprises a TACI receptor immunoadhesin.  
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4. The method of claim 3 wherein said TACI receptor immunoadhesin comprises a TACI extracellular domain sequence fused to an Fc region of an immunoglobulin.

20 5. The method of claim 1 wherein said TALL-1 polypeptide antagonist comprises a BCMA receptor immunoadhesin.

6. The method of claim 5 wherein said BCMA receptor immunoadhesin comprises a BCMA extracellular domain sequence fused to  
25 an Fc region of an immunoglobulin.

7. The method of claim 1 wherein said TALL-1 polypeptide antagonist comprises a TACI receptor variant.

30 8. The method of claim 1 wherein said TALL-1 polypeptide antagonist comprises a BCMA receptor variant.

9. The method of claim 1 wherein said TALL-1 polypeptide antagonist comprises a TACI receptor linked to a nonproteinaceous  
35 polymer selected from the group consisting of polyethylene glycol, polypropylene glycol, and polyoxyalkylene.

10. The method of claim 1 wherein said TALL-1 polypeptide antagonist comprises a BCMA receptor linked to a nonproteinaceous polymer selected from the group consisting of polyethylene glycol, polypropylene glycol, and polyoxyalkylene.

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11. The method of claim 1 wherein said TALL-1 polypeptide antagonist comprises a TACI receptor polypeptide or BCMA receptor polypeptide linked to a heterologous sequence.

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12. The method of claim 11 wherein said heterologous sequence is an epitope tag sequence.

13. The method of claim 11 wherein said heterologous sequence is a leucine zipper sequence.

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14. The method of claim 1 wherein said TALL-1 polypeptide antagonist comprises an antibody selected from the group consisting of a TACI receptor antibody, a BCMA receptor antibody, a TALL-1 polypeptide antibody and an APRIL polypeptide antibody.

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15. The method of claim 1 wherein said TALL-1 polypeptide antagonist comprises an extracellular domain sequence of TACI receptor or an extracellular domain sequence of BCMA receptor.

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16. The method of claim 1 wherein said TALL-1 polypeptide antagonist comprises an antagonist molecule which inhibits or neutralizes both TALL-1 polypeptide and APRIL polypeptide biological activity in mammalian cells.

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17. The method of claim 1 wherein said mammalian cells comprise white blood cells.

18. A method of inhibiting or neutralizing TALL-1 polypeptide biological activity in mammalian cells, comprising exposing said mammalian cells to an effective amount of an antagonist which inhibits or neutralizes a biological activity of a native sequence TALL-1 polypeptide having the amino acid sequence of Figure 3 (SEQ ID NO:6) or a fragment thereof.

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19. A method of inhibiting or neutralizing APRIL polypeptide biological activity in mammalian cells, comprising exposing said mammalian cells to an effective amount of APRIL polypeptide antagonist.

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20. The method of claim 19 wherein said APRIL polypeptide comprises a native sequence APRIL polypeptide having the amino acid sequence of Figure 4 (SEQ ID NO:8) or a fragment thereof which exhibits a biological activity of the native sequence APRIL polypeptide shown in Figure 4 (SEQ ID NO:8).

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21. The method of claim 19 wherein said APRIL polypeptide antagonist comprises a TACI receptor immunoadhesin.

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22. The method of claim 21 wherein said TACI receptor immunoadhesin comprises a TACI extracellular domain sequence fused to an Fc region of an immunoglobulin.

23. The method of claim 19 wherein said APRIL polypeptide antagonist comprises a BCMA receptor immunoadhesin.

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24. The method of claim 23 wherein said BCMA receptor immunoadhesin comprises a BCMA extracellular domain sequence fused to an Fc region of an immunoglobulin.

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25. The method of claim 19 wherein said APRIL polypeptide antagonist comprises a TACI receptor variant.

26. The method of claim 19 wherein said APRIL polypeptide antagonist comprises a BCMA receptor variant.

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27. The method of claim 19 wherein said APRIL polypeptide antagonist comprises a TACI receptor linked to a nonproteinaceous polymer selected from the group consisting of polyethylene glycol, polypropylene glycol, and polyoxyalkylene.

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28. The method of claim 19 wherein said APRIL polypeptide antagonist comprises a BCMA receptor linked to a nonproteinaceous polymer selected from the group consisting of polyethylene glycol, polypropylene glycol, and polyoxyalkylene.

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29. The method of claim 19 wherein said APRIL polypeptide antagonist comprises a TACI receptor polypeptide or BCMA receptor polypeptide linked to a heterologous sequence.

5 30. The method of claim 29 wherein said heterologous sequence is an epitope tag sequence.

31. The method of claim 29 wherein said heterologous sequence is a leucine zipper sequence.

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32. The method of claim 19 wherein said APRIL polypeptide antagonist comprises an antibody selected from the group consisting of a TACI receptor antibody, a BCMA receptor antibody, a TALL-1 polypeptide antibody and an APRIL polypeptide antibody.

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33. The method of claim 32 wherein said APRIL polypeptide antagonist comprises the anti-APRIL antibody 3C6.4.2 deposited as ATCC accession number PTA-1347.

20 34. The method of claim 19 wherein said APRIL polypeptide antagonist comprises an extracellular domain sequence of TACI receptor or an extracellular domain sequence of BCMA receptor.

35 35. The method of claim 19 wherein said APRIL polypeptide antagonist comprises an antagonist molecule which inhibits or neutralizes both TALL-1 polypeptide and APRIL polypeptide biological activity in mammalian cells.

30 36. The method of claim 19 wherein said mammalian cells comprise white blood cells.

37. A method of inhibiting or neutralizing APRIL polypeptide biological activity in mammalian cells, comprising exposing said mammalian cells to an effective amount of an antagonist which  
35 inhibits or neutralizes a biological activity of a native sequence APRIL polypeptide having the amino acid sequence of Figure 4 (SEQ ID NO:8) or a fragment thereof.

38. A method of enhancing or stimulating TACI polypeptide activity in mammalian cells, comprising exposing said mammalian cells to an effective amount of TACI polypeptide agonist.

5 39. The method of claim 38 wherein said TACI polypeptide agonist comprises an anti-TACI agonist antibody.

40. The method of claim 38 wherein said TACI polypeptide agonist mimics the activity of APRIL polypeptide or TALL-1 polypeptide.

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41. A method of enhancing or stimulating BCMA polypeptide activity in mammalian cells, comprising exposing said mammalian cells to an effective amount of BCMA polypeptide agonist.

15 42. The method of claim 41 wherein said BCMA polypeptide agonist comprises an anti-BCMA agonist antibody.

43. The method of claim 41 wherein said BCMA polypeptide agonist mimics the activity of APRIL polypeptide or TALL-1 polypeptide.

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44. A method of treating a TALL-1 -related pathological condition in a mammal, comprising administering to said mammal an effective amount of TALL-1 antagonist.

25 45. The method of claim 44 wherein said TALL-1 antagonist is selected from the group consisting of a soluble, extracellular domain sequence of TACI or BCMA, TACI receptor immunoadhesin, BCMA receptor immunoadhesin, TACI receptor variant, BCMA receptor variant, pegylated TACI receptor, pegylated BCMA receptor, TACI receptor  
30 fusion protein, BCMA receptor fusion protein, TACI antibody, BCMA antibody, TALL-1 antibody, and APRIL antibody.

46. The method of claim 44 wherein said pathological condition is an immune related disease.

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47. The method of claim 46 wherein said immune related disease is an autoimmune disease.

48. The method of claim 46 wherein said immune related disease  
40 comprises rheumatoid arthritis.

49. The method of claim 44 wherein said pathological condition is multiple sclerosis.

5 50. The method of claim 44 wherein said pathological condition is cancer.

51. The method of claim 50 wherein said cancer is leukemia, lymphoma, or myeloma.

10 52. The method of claim 50 wherein said cancer is colon, lung, or melanoma cancer.

15 53. The method of claim 44 wherein, in addition to administering said TALL-1 antagonist, one or more cytotoxic agents, chemotherapeutic agents, cytokines, or growth inhibitory agents are administered to said mammal.

20 54. A method of treating an APRIL-related pathological condition in a mammal, comprising administering to said mammal an effective amount of APRIL antagonist.

25 55. The method of claim 54 wherein said APRIL antagonist is selected from the group consisting of a soluble, extracellular domain sequence of TACI or BCMA, TACI receptor immunoadhesin, BCMA receptor immunoadhesin, TACI receptor variant, BCMA receptor variant, pegylated TACI receptor, pegylated BCMA receptor, TACI receptor fusion protein, BCMA receptor fusion protein, TACI antibody, BCMA antibody, TALL-1 antibody, and APRIL antibody.

30 56. The method of claim 54 wherein said pathological condition is an immune related disease.

35 57. The method of claim 56 wherein said immune related disease is an autoimmune disease.

58. The method of claim 56 wherein said immune related disease comprises rheumatoid arthritis.

59. The method of claim 54 wherein said pathological condition is multiple sclerosis.

5 60. The method of claim 54 wherein said pathological condition is cancer.

61. The method of claim 60 wherein said cancer is leukemia, lymphoma, or myeloma.

10 62. The method of claim 54 wherein, in addition to administering said TALL-1 antagonist, one or more cytotoxic agents, chemotherapeutic agents, cytokines, or growth inhibitory agents are administered to said mammal.

15 63. A composition comprising a TALL-1 polypeptide antagonist and a carrier.

20 64. The composition of claim 63 wherein said carrier comprises a pharmaceutically acceptable carrier.

65. A composition comprising an APRIL antagonist and a carrier.

25 66. The composition of claim 65 wherein said carrier comprises a pharmaceutically acceptable carrier.

67. A monoclonal antibody which specifically binds to APRIL polypeptide and blocks binding of said APRIL polypeptide to a TACI receptor or a BCMA receptor.

30 68. The monoclonal antibody of claim 67 which further blocks binding of said APRIL polypeptide to a TACI receptor and a BCMA receptor.

35 69. The monoclonal antibody of claim 67 wherein said monoclonal antibody comprises the 3C6.4.2 antibody secreted by the hybridoma deposited with ATCC as accession number PTA-1347.

70. A monoclonal antibody which binds to the same epitope as the epitope to which the 3C6.4.2 monoclonal antibody produced by the hybridoma cell line deposited as ATCC accession number PTA-1347 binds.

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71. The hybridoma cell line which produces monoclonal antibody 3C6.4.2 and deposited with ATCC as accession number PTA-1347.

72. The monoclonal antibody 5E11.1.2 secreted by the hybridoma deposited with ATCC as accession number PTA-1346.

73. A monoclonal antibody which binds to the same epitope as the epitope to which the 5E11.1.2 monoclonal antibody produced by the hybridoma cell line deposited as ATCC accession number PTA-1346 binds.

74. The hybridoma cell line which produces monoclonal antibody 5E11.1.2 and deposited with ATCC as accession number PTA-1346.

75. The monoclonal antibody 5G8.2.2 secreted by the hybridoma deposited with ATCC as accession number PTA-1345.

76. A monoclonal antibody which binds to the same epitope as the epitope to which the 5G8.2.2 monoclonal antibody produced by the hybridoma cell line deposited as ATCC accession number PTA-1345 binds.

77. The hybridoma cell line which produces monoclonal antibody 5G8.2.2 and deposited with ATCC as accession number PTA-1345.

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78. The monoclonal antibody 5E8.7.4 secreted by the hybridoma deposited with ATCC as accession number PTA-1344.

79. A monoclonal antibody which binds to the same epitope as the epitope to which the 5E8.7.4 monoclonal antibody produced by the hybridoma cell line deposited as ATCC accession number PTA-1344 binds.

80. The hybridoma cell line which produces monoclonal antibody 5E8.7.4 and deposited with ATCC as accession number PTA-1344.

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81. A chimeric anti-APRIL antibody which specifically binds to APRIL polypeptide and comprises a sequence derived from the 3C6.4.2 antibody secreted by the hybridoma deposited with ATCC as accession number PTA-1347.

82. A chimeric anti-APRIL antibody which specifically binds to APRIL polypeptide and comprises a sequence derived from the 5E11.1.2 antibody secreted by the hybridoma deposited with ATCC as accession number PTA-1346.

83. A chimeric anti-APRIL antibody which specifically binds to APRIL polypeptide and comprises a sequence derived from the 5G8.2.2 antibody secreted by the hybridoma deposited with ATCC as accession number PTA-1345.

84. A chimeric anti-APRIL antibody which specifically binds to APRIL polypeptide and comprises a sequence derived from the 5E8.7.4 antibody secreted by the hybridoma deposited with ATCC as accession number PTA-1344.

85. A humanized anti-APRIL antibody which specifically binds to APRIL polypeptide and comprises a sequence derived from the 3C6.4.2 antibody secreted by the hybridoma deposited with ATCC as accession number PTA-1347.

86. A humanized anti-APRIL antibody which specifically binds to APRIL polypeptide and comprises a sequence derived from the 5E11.1.2 antibody secreted by the hybridoma deposited with ATCC as accession number PTA-1346.

87. A humanized anti-APRIL antibody which specifically binds to APRIL polypeptide and comprises a sequence derived from the 5G8.2.2 antibody secreted by the hybridoma deposited with ATCC as accession number PTA-1345.

88. A humanized anti-APRIL antibody which specifically binds to APRIL polypeptide and comprises a sequence derived from the 5E8.7.4 antibody secreted by the hybridoma deposited with ATCC as accession number PTA-1344.